(19) Japanese Patent Office (JP) (12) PATENT JOURNAL (A) (11) Kokai Patent Application No. Hei 6[1994]-56676

(43) Publication Date: March 1, 1994

(51) Int. Cl.[5]:	Identification Code	JPO File No.
A61K 31/78	ABN	8314-4C
9/107		Z 7329-4C

Examination Request: Not requested No. of Claims: 1 (Total of 8 pages)

(21) Application No.: Hei 4[1992]-250360

(22) Application Date: August 5, 1992

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(54) SUSPENSION FOR BLOOD VESSEL EMBOLIZATION

(57) **Abstract**
[Purpose] To provide a suspension for blood vessel embolization to be injected through a catheter for occluding specific parts of the blood vessel.
[Constitution] A suspension for blood vessel embolization is prepared by suspending a high water-absorbing resin particles which are mainly made of a polymer of sodium acrylate or a polymer of sodium acrylate and vinyl alcohol and have an average grain size of less than about 1.0 mm in an oily contrast medium.

CLAIM

1. A suspension for blood vessel embolization, prepared by suspending a high water-absorbing resin particles that are mainly made of a polymer of sodium acrylate, or a polymer of sodium acrylate and vinyl alcohol, and have an average grain size of less than about 1.0 mm in an oily contrast medium.

DETAILED EXPLANATION OF THE INVENTION

[0001]

Industrial application field

This invention relates to a suspension for blood vessel embolization. More specifically, it relates to a suspension for blood vessel embolization to be injected through a catheter for occluding specific parts of the blood vessel.

[0002]

Prior art and the problems to be solved by the invention

Cyanoacrylates (isobutyl-2-cynoacrylate, n-butyl cyanoacrylate) used in arterial embolectomy, in particular, embolectomy for arteriovenous malformation in the cranium were recognized conventionally as effective embolic materials. However, there were demerits such as requiring experience in carrying out adjustment of the concentration for polymerizing in the nidus (the shunt section of the arteriovenous malformation), causing occlusion of the catheter at times due to polymerizing in the catheter, having a danger of the catheter and the polymerized cyanoacrylates adhering, etc. A method of injecting a small amount of cyanoacrylate by dividing into a number of times has been proposed in order to solve the problem of adhesion. However, close attention was still necessary. EVAL (Ethylene Vinyl Alcohol copolymer) is being used at many facilities in order to compensate for the demerits in these cyanoacrylates. However, an organic solvent is necessary and there are cases when the compatibility with the catheter is poor hence development of an embolic material that is easy to handle and is not toxic is desired. On the other hand, there have been many reports of using Polyvinyl Alcohol (PVA) and suture yarn as the embolic material. However, these occlude the catheter at times and furthermore, the artery occludes at the center side hence a material with a high re-opening rate of the arteriovenous malformation and capable of carrying out occlusion at a place as close to the nidus as possible is desired. To achieve this object, it is necessary to contrive a way to use by mixing an Ethanol or Avitene (microfibrillarcollaten). Therefore, being able to pass through a very fine catheter, having a favorable contrast property, not passing through the nidus, having a permanent occlusion effect, not being toxic, etc. can be cited as the conditions required in the embolic material in relation to embolectomy within the cranium.

[0003]

Means of solving the problems and the operation of the invention

This invention is a suspension for blood vessel embolization prepared by suspending a high water-absorbing resin particles that are mainly made of a polymer of sodium acrylate, or a

polymer of sodium acrylate and vinyl alcohol and have an average grain size of less than about 1.0 mm in an oily contrast medium. Namely, this invention causes the blood vessel to function as an embolic material by employing the fact that high water-absorbing resin particles absorb water and instantaneously swell (e.g., swell by absorbing the moisture content at 1000 fold of the self weight) by coming into contact with moisture content, namely, blood (moisture content therein). Furthermore, the aforementioned water absorption and swelling is delayed by suspending the high water absorbing resin particles in an oily contrast medium so that the function as an embolic material occurs only in the necessary area of the blood vessel and not in the area adjacent to the catheter or inside the catheter.

[0004]

The principal component of the high water-absorbing resin particles used in this invention is a polymer of sodium acrylate, or a polymer of sodium acrylate and vinyl alcohol. In particular, saponified substance of vinyl acetate–acrylic acid ester copolymer, saponified substance of vinyl acetate–maleic acid methyl, cross-linked substance of isobutylene–maleic acid anhydride copolymer, saponified substance of starch–acryl nitrile graft copolymer, cross-linked sodium polyacrylate, and cross-linked substance of polyethylene oxide, etc. can be cited as specific examples.

[0005]

As these high water-absorbing resin particles, those with an average grain size of less than about 1.0 mm, preferably, less than 0.9 mm are used. Furthermore, the necessary parts of the blood vessel can be occluded by suitably selecting the average grain size of these particles.

[0006]

In this invention, a suspension is prepared by suspending these high water-absorbing resin particles in an oily contrast medium. In this case, it is preferable to suspend 10 ~ 20 mg of the high water-absorbing resin particles to 1 ml of the oily contrast medium. As this oily contrast medium, a contrast medium [Lipiodol (registered trade name)] prepared from iodized saponification oil fatty acid ether ester, a contrast medium [Urografin (registered trade name)] containing amidotrizoic acid (as an anhydride), sodium hydroxide, and meglumine, a contrast medium [Angiografin (registered trade name)] containing amidotrizoic acid (as an anhydride) and meglumine, etc. can be cited. When the suspension obtained is injected into the specific part (e.g., artery) of the blood vessel according to a catheter, the high water-absorbing resin particles flow to the periphery of the blood vessel and here the oily part of the coat separates and absorbs

the moisture content the instant (e.g., 2 ~ 3 seconds) contact is made with the moisture content in the blood, increases the diameter (e.g., 4.5 fold), and functions as an embolic material.

[0007]

A use example of the suspension for blood vessel embolization related to this invention will be cited below.

[0008] a) Occlusion example of malignant tumor

Poor blood vessel Suspension (10 mg/ml) of N-100 (S) and Lipiodol

Rich blood vessel Suspension (10 mg/ml) of N-100 (M) or N-100 (L) and Lipiodol

N-100 and S-50 were mixed to prepare a suspension of Lipodol (10 ~ 15 mg/ml). However, N-100: sodium acrylate polymer, S-50: acrylic acid · vinyl alcohol copolymer, (S) (M) (L) indicate the size of the particles and are 0.20 mmϕ, 0.53 mmϕ, 0.88 mmϕ respectively as the average grain size.

[0009]

b) Occlusion example of arteriovenous aneurysm (AVM)

Low Flow Type: Suspension (10 mg/ml) of N-100 (S) and Lipiodol

High Flow type: Mix N-100 and S-50 to prepare a suspension of Lipiodol (10 ~ 15 mg/ml)

[0010]

c) Occlusion example of arterial hemorrhage

few each of S-50 having a larger diameter than the diameter of the hemorrhaging blood vessel were counted and suspended along with the contrast medium, and then, this suspension was injected until the hemorrhaging stops.

[0011]

Working Example 1

A blood vessel embolization model (1) was prepared as shown in Figure 1 wherein arteriovenous aneurysm was presupposed in order to verify that the suspension for blood vessel embolization related to this invention actually has an occlusion effect. Blood vessel embolization model (1) was prepared by filling urethane foam sponge (continuous foam) (3) of cylindrical shape (height 2 mm, diameter 18 mm) in a plastic chamber (2) having a capacity of about 2.0 ml. The blood passes through this chamber (2) without any resistance. A 500 ml ~ 1,000 ml bottle (4) of physiological saline solution was connected to this blood vessel embolization model (1),

constant pressure of 150 mmHg was applied to this bottle using an automatic pressurizing apparatus (5), and steady flow was fluidized in chamber (2). Incidentally, (6) is the manometer and (7) the microcatheter. The two kinds indicated below were filled as the urethane foam sponge. Namely,

Low flow type: Each bubble in the urethane foam Average 0.5 mm

High flow type: Each bubble in the urethane foam Average 0.9 mm

The occlusion effect was judged by measuring the flow rate of the physiological saline solution.

[0012]

a) Occlusion of low flow type AVM model (refer to Figure1, Figure 2, and Figure 4)

When a suspension of (N-100) (S) 76% Urografin and Lipiodol mixture was used, the flow stopped at N-100 (S) 40 mg. On the other hand, when N-100 (M) was used, the flow stopped at 5 mg or less with the same suspension. There is a tendency to clog the greater the amount of N-100 is and the larger its grain size is.

[0013]

b) Occlusion of high flow type AVM model (refer to Figure 1, Figure 2, and Figure 5)

Occlusion effect was not recognized in a suspension of N-100 (M) 76% Urografin and Lipiodol mixture. Occlusion effect appears by adding S-50 (M). Occlusion effect appears at a small amount of 10 mg with N-100 (L) + S-50 (L). There is no occlusion effect with N-100 (S) + S-50 (S). Even with N-100 (S) + S-50 (S), the S-50 particles become large when suspended with Angiografin and has occlusion effect. According to these data, it is very important to mix S-50 for occlusion of AVM of fast blood flow.

[0014]

Clinical example

a) 26 years old female Metrorrhagia after abortion

Photograph of the pelvic artery: Expansion of the right uterine artery and abnormal blood vessel that had expanded in a spiral shape in correspondence with the uterus were recognized. Leakage of the contrast medium to outside the blood vessel was also recognized and hemorrhaging was also confirmed.

Selective right uterine artery (after embolectomy): S-50 (M) 5 mg was absorbed with physiological saline water, suspended in Lipiodol, injected according to a catheter, and photographed. The abnormal blood vessel was eliminated, leakage of the contrast medium to the

outside of the flood vessel was no longer recognized, and only the normal uterine artery muscle was extracted. After the embolectomy, hemorrhaging from the uterus stopped.

The following cited the characteristics as an embolic material when using the suspension for blood vessel embolization related to this invention.

a) No toxicity · irritation: With regards to this, data already exist. When conjectured from past research on the tissue reaction of embolic material, it does not pose a problem in particular. There was no pain during the injection in 10 clinical cases.

b) Low viscosity: It is slightly higher than the viscosity of Lipiodol and unless it is a suspension of very high concentration, it can be passed through a micro-catheter with a 1.0 ml syringe.

c) Favorable contrast property: Lipiodol is used as the suspension hence it is possible to see right through. The occlusion effect can be confirmed due to the Lipiodol accumulating in the occlusion part.

d) Does not occlude the catheter: The particles do not coagulate hence it does not clog the catheter. It does not have adhesiveness hence there is no danger of adhering the catheter and the blood vessel.

e) The occlusion part can be adjusted: The size of the particles can be adjusted. The method is to adjust with (S) (M) (L), or adjust the size of the particles according to the contrast medium to be suspended. Based on this, it is possible to determine the blood vessel diameter that can be occluded in advance.

[0015]

Effects of the invention

By using the suspension for blood vessel embolization related to this invention, there are the effects of not having toxicity · irritation, the viscosity being low, the contrast property being favorable, the catheter not being occluded, and being able to adjust the occlusion part.

BRIEF DESCRIPTION OF THE INVENTION

1. It is an explanatory diagram showing the amount of fluid that N-100 (10 mg) can absorb.

2. It is an explanatory diagram showing the change in the diameter of S-50 in various fluids.

3. It is an explanatory diagram showing the whole assembly of an AVM model.

4. It is a graph showing the occlusion effect of a Low Flow Model.

5. It is a graph showing the occlusion effect of a High Flow Model.

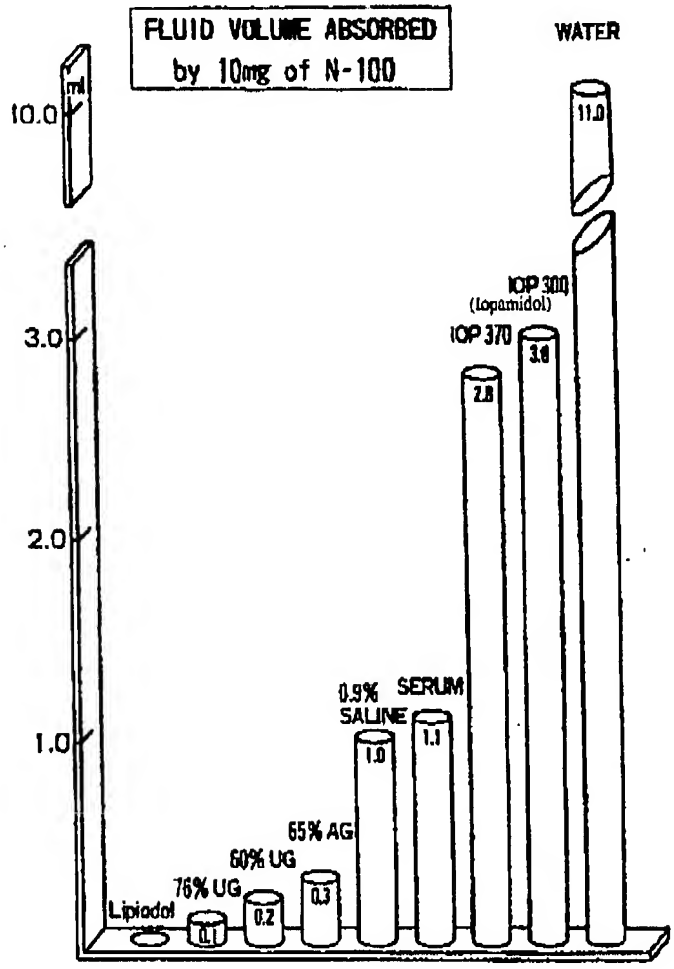

Figure 1

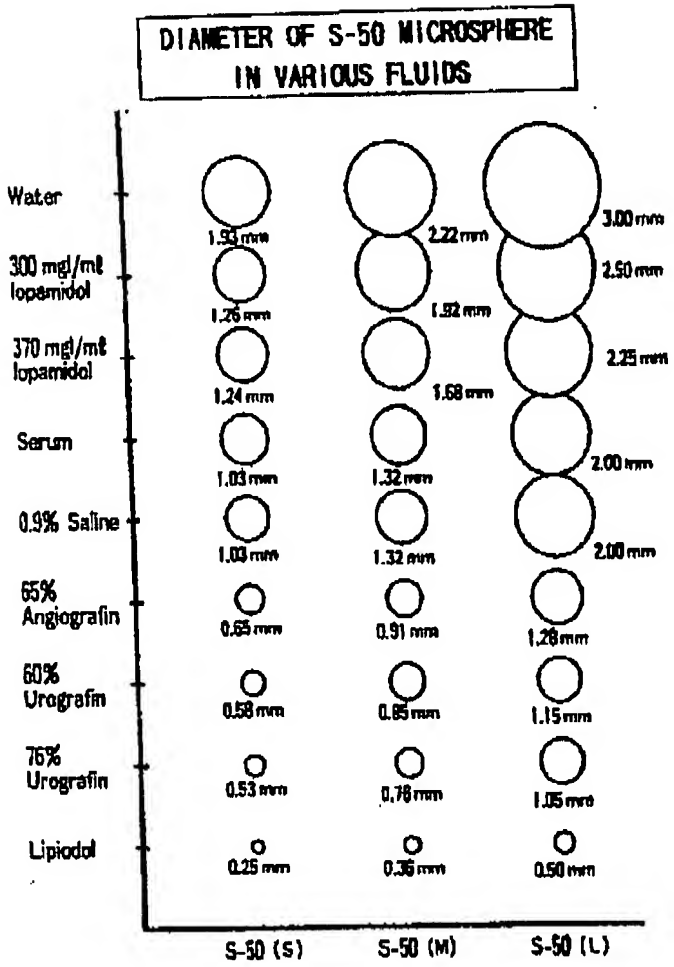
DIAMETER OF S-50 MICROSPHERE IN VARIOUS FLUIDS
Water
300 mgI/ml Iopamidol
370 mgI/ml Iopamidol
Serum
0.9% Saline
65% Angiografin
60% Urografin
76% Urografin
Lipiodol
1.93 mm
2.22 mm
3.00 mm
1.26 mm
1.92 mm
2.50 mm
1.24 mm
1.68 mm
2.25 mm
1.03 mm
1.32 mm
2.00 mm
1.03 mm
1.32 mm
2.00 mm
0.65 mm
0.91 mm
1.28 mm
0.58 mm
0.85 mm
1.15 mm
0.53 mm
0.78 mm
1.05 mm
0.25 mm
0.36 mm
0.50 mm
S-50 (S)
S-50 (M)
S-50 (L)

Figure 2

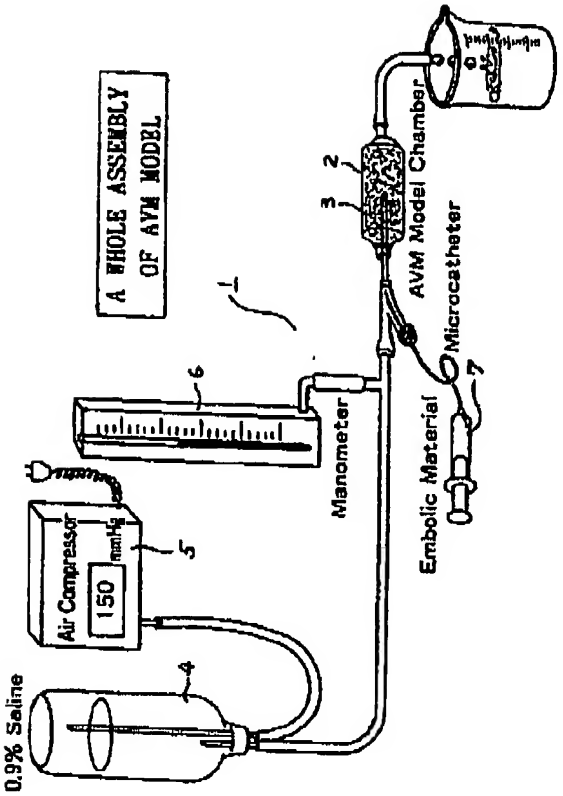

Figure 3

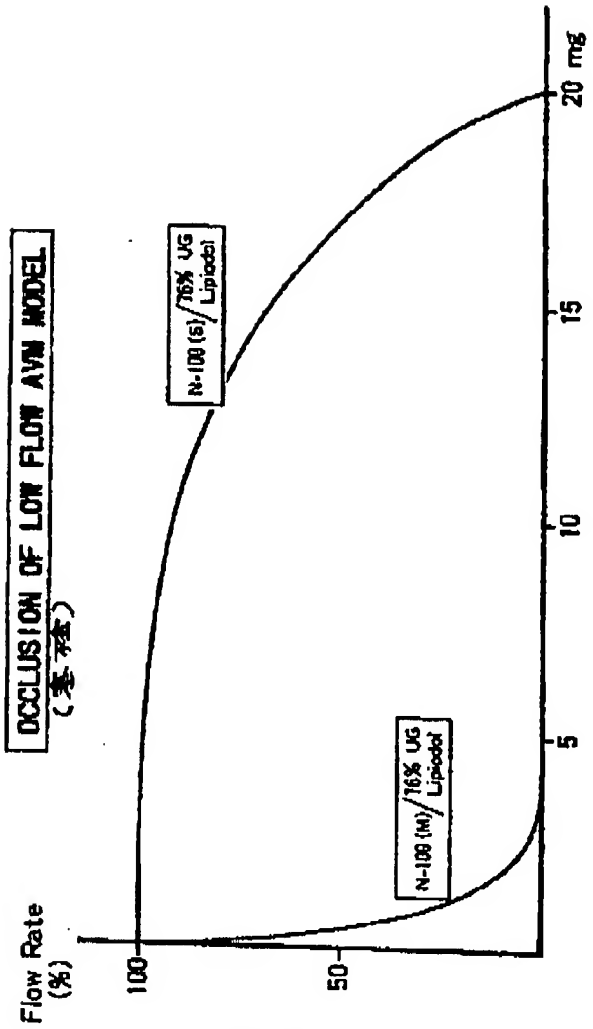

Figure 4

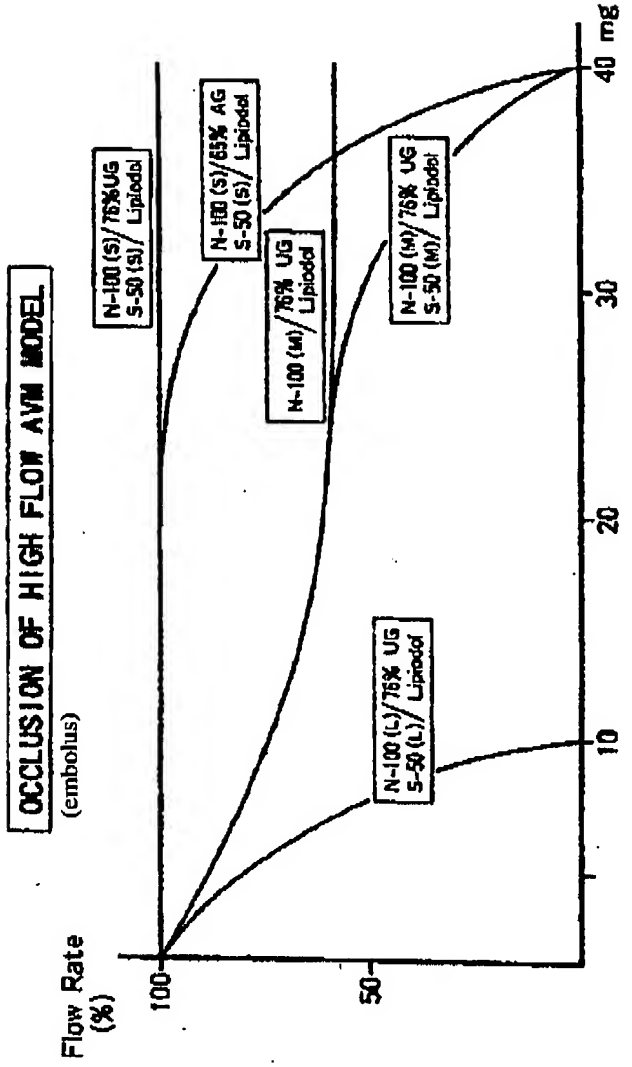

Figure 5

Translated by:

PHOENIX TRANSLATIONS

September 13, 2007

132-14552